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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/036,819	03/09/1998	A. SAID EL SHAMI	107-145D-C	6406

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER

1645 21
DATE MAILED: 04/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/036,819	Applicant(s) El Shami
Examiner S. Devi, Ph.D.	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on Mar 15, 2002
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 54 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) _____ is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims 54 are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

- a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). _____
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) Other: _____

DETAILED ACTION

After-Final Amendment

- 1) Acknowledgment is made of Applicant's After-Final amendment filed 03/15/02 (paper no. 20) in response to the Final rejection mailed 09/04/01 (paper no. 16). The amendment has been entered.

Status of Claims

- 2) Claim 54 has been amended via the amendment filed 03/15/02.
Claim 54 is pending and under examination.

Finality Withdrawn

- 3) The finality of the Office Action mailed 09/04/01 (paper no. 16) is hereby withdrawn. Applicant is asked to note the new grounds of rejections made below.

Prior Citation of Title 35 Sections

- 4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

- 5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

- 6) The objection to claim 10 made in paragraph 10 of the Office Action mailed 09/04/01 (paper no. 16) is withdrawn in light of Applicant's amendment to the claim.

Objection(s) Maintained

- 7) The objection to the specification made in paragraph 5(b) of the Office Action mailed 02/04/99 (paper no. 4) and maintained in paragraph 8 of the final Office Action mailed 06/24/99 (paper no. 6) is maintained for reasons set forth therein. Although Applicant has replaced Tables 20-25 via the amendment filed 04/12/99 (paper no. 5), the rest of the Tables and related text have not been amended. However, Applicant assures the Office that the specification would be appropriately edited upon indication of allowance.

Rejection(s) Withdrawn

- 8) The rejection of claim 54 made in paragraphs 9(a) and 9(b) of the Office Action mailed 09/04/01 (paper no. 16) under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

Rejection(s) Maintained

- 9) The rejection of claim 54 made in paragraph 8 of the Office Action mailed 09/04/01 (paper no. 16) under 35 U.S.C. 112, first paragraph, as containing new matter, is maintained for reasons set forth therein and herebelow.

Claim 54, as amended, includes the following newly added limitations as shown below in bold:

54. A method for determining the concentration of the free **portion of** testosterone ligand in a biological fluid, wherein said free **portion of** testosterone is in equilibrium with another **portion of** testosterone bound to one or more endogenous binders in said fluid comprising the steps of (a) forming a mixture of a sample of said fluid with (1) an amount of a specific antibody for the free portion of testosterone **insufficient to substantially affect** said equilibrium, and (2) a labeled analog of testosterone which is radioiodinated 6-hydroxy-testosterone-19-carboxymethyl ether histamine that binds to said antibody and has affinity for the endogenous binders lower than that of the **free portion of** testosterone for said endogenous binders, (b) maintaining said mixture to permit said labeled analog to compete with the **free portion of** testosterone for binding with the antibody, (c) measuring the amount of said labeled analog that has, or has not, become bound to the antibody, and (d) determining the concentration of the **free portion of** testosterone from said measurement, wherein the improvement comprises including in the mixture an amount of a blocking agent which is sulfobromophthalein to inhibit the binding of said labeled analog to the endogenous binders without displacing testosterone bound to said endogenous binders.

- 10) The rejection of claim 54 made in paragraph 9(c) of the Office Action mailed 09/04/01 (paper no. 16) under 35 U.S.C. 112, second paragraph, as being indefinite, is maintained for the reason set forth therein and herebelow.

Applicant contends that the term "substantially" no longer appears in the claim. However, the amended claim still includes the limitation "substantially affect" in line 5.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

- 11) Claim 54 is rejected under 35 U.S.C §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 54 lacks proper antecedent basis for the recitation "displacing "testosterone" (see line 2 from the bottom of the claim). The earlier part of the claim recites two types of

testosterone: a free portion of testosterone and another portion of testosterone. It is unclear which testosterone does the above-identified limitation represent.

Rejection Based on the Lost Interference Count

12) In accordance with the practice set out in M.P.E.P 2363, claims 54 is rejected under 35 U.S.C § 103 as being unpatentable over the count of Interference no. 101,933.

The count 1 of Interference no. 101,933 is provided below:

In a method of determining the concentration of a free portion of a ligand in a biological fluid, wherein said free ligand is in equilibrium with another portion of the ligand bound to one or more endogenous binders in said fluid comprising the steps of (a) forming a mixture of a sample of said fluid with (1) an amount of a specific binder for the free ligand insufficient to substantially affect said equilibrium, and (2) a labeled derivative of the ligand that binds to said specific binder and has affinity for the endogenous binders lower than that of the ligand for said endogenous binders, (b) maintained said mixture to permit the ligand derivative to complete with the free ligand for binding with the specific binder, (c) measuring the amount of ligand derivative that has, or has not, become bound to the specific binder, and (d) determining the concentration of said free ligand from said measurement, wherein the improvement comprises including in the mixture an amount of a blocking agent which substantially reduces the binding of the ligand derivative to the endogenous binders without substantially reducing the binding of the ligand to said endogenous binders.

The count clearly embraces the use of a specific binding ligand in a method of determining or measuring the concentration of any free ligand in a biological fluid. The free ligand, the specific ligand binder and the blocking agent recited in the count are inclusive of the subgenus ligand, testosterone; the subgenus specific ligand binder, antibody; and the subgenus blocking agent, sulfobromophthalein. The labeled analog now included in claim 54 is subgeneric to the labeled derivative recited in the count. Therefore, the instant claim 54 is unpatentable or obvious over the count of Interference no. 103,933.

It is noted that a similar rejection made in the parent case, SN 07/303,712, was affirmed by the Board. In this prior application SN 07/303,712, claim 32 included the limitation “sulfobromoophthalein” and claim 34 included the limitation “testosterone ligand”. In affirming the Examiner’s rejection via the Decision mailed 01/09/1998, the Board noted the Appellant’s acknowledgment that his claims, i.e., claims 28-34 in SN 07/303,712, were subgeneric to the count. The Board also noted Appellant’s indication that what made claims 28-34 different from the interference count was the recitation of an affinity constant for the specific binding ligand: “up to at least 5×10^5 l/mol”. The Board noted the Appellant’s argument that this recitation of

the affinity constant was “critical”. It is noted now that the recitation of this affinity constant is absent in the instant claim 54 in the instant application, SN 09/036,819, which is a continuation application of SN 07/303,712. The Board also noted in the parent application that when an Applicant has conceded that he/she is not entitled to a patent for the subject matter embraced in the interference counts, claims thereafter presented must be “inventive different” from the interference counts. *In re Cole*, 82 F.2d 405, 407, 29 USPQ 137, 139 (CCPA 1936); citing, *In re Dodge*, 74 F.2d 756, 757-758, 24 USPQ 219, 229 (CCPA 1935). By Applicants’ own previous account or acknowledgment and the Board’s decision, it is apparent that the subject matter of instant claim 54 does not differ from that of the interference count.

The instant application SN 09/036,819 is a continuation of SN 07/303,712, which in turn is a Divisional of application SN 06/784,857. It is noted that a judgment adverse to El Shami was rendered by the Board of Patent Appeals and Interferences in application SN 06/784,857, claim 18 of which included the limitation “iodinated 6-hydroxytestosterone-19-carboxymethyl ether histamine analog”; claims 17 of which included the limitation “testosterone ligand”; claim 10 of which included the limitation “antibody to said free ligand”; and claim 23 of which included the limitation “sulfobromophthalein”. It is further noted that claims 1-27 of the application SN 06/784,857 corresponded to the count of the Interference No. 101,933.

Rejection Based on Public Use and Sale - 35 U.S.C § 102(b) / 103

13) Claim 54 is rejected based upon the public use or sale of the invention, i.e., Salicylate Kits and of Immunoassay kits.

The instant application SN 09/036,819 is a continuation of SN 07/303,712, which in turn is a Divisional of application SN 06/784,857. It is noted that a judgment adverse to El Shami was rendered by the Board of Patent Appeals and Interferences in application SN 06/784,857, claim 18 of which included the limitation “iodinated 6-hydroxytestosterone-19-carboxymethyl ether histamine analog”; claim 17 of which included the limitation “testosterone ligand”; claim 10 of which included the limitation “antibody to said free ligand”; and claim 23 of which included the limitation “sulfobromophthalein”. It is further noted that claims 1-27 of the application SN 06/784,857 corresponded to the count of the Interference No. 101,933, and all these claims, i.e., claims 1, 10, 17, 18 and 23 included, were held unpatentable under 35 U.S.C. §

102(b) / 103 on the grounds of public use and sale. Instant claim 54, which includes these limitations, is rejected on the same basis. See also paragraph 10 of the previous Office Action mailed 02/04/99 (paper no. 4).

Relevant Prior Art

14) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicant's disclosure:

- Felicetta *et al.* (*J. Clin. Endocrinol. Metabolism* 57: 207-212, 1983) teach the use of sulfobromophthalein (BSP) as a blocking agent which displaces a ligand bound to serum proteins (see entire document).
- Amino *et al.* (*Clin. Chem.* 29: 321-325, 1983) teach the effect of serum albumin concentration on the assay of serum free thyroxin by equilibrium radioimmunoassay with labeled thyroxin analog (see entire document).
- Tabachnick *et al.* (*Arch. Biochem. Biophys.* 136: 467-479, 1970) teach the structural requirements for binding of benzene derivatives to thyroxine-binding sites on human serum albumin (see entire document).

Remarks

15) Claim 54 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

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If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

April 2002

SD
S. DEVI, PH.D.
PRIMARY EXAMINER